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Before the Acquisition Advisory Panel

Chairwoman Madsen, members of the panel, thank you for this opportunity to appear before you today.

The federal government spends more than $320 billion on products and services each year. As a market actor the federal government purchases everything from soup to nuts—literally—along with consulting services, advanced communications technologies, and futuristic weapons systems.

Today, however, I want to talk about a relatively small, yet highly innovative component of that marketplace: the $5.6 billion, multi-year BioShield program. While this program may be relatively small in size compared with the cost of a new fleet of aircraft carriers or wing of stealth bombers, this program may be the most important step we can take in better securing the United States against a terrorist attack using weapons of mass destruction (WMD).

I. Overview of the BioShield Program—A Groundbreaking Concept

The theory behind BioShield is elegant in its simplicity: If we can find cures to counter the weapons of mass destruction a terrorist may use against us, the ability of a terrorist to do great harm to our nation is significantly diminished. Every weapon of mass destruction—nuclear, biological, chemical and radiological—we can counter is an arrow taken out of the terrorists quiver.

This capability is particularly important in this era of asymmetrical threats where terrorists don't leave return addresses and where small, non-state actors with no military to speak of can inflict immense harm if they have access to the right weapons. Radiation from a nuclear or dirty bomb penetrates the best armor. You can't outgun a microbe. We need medical counter-measures to these threats.

Consider the example of Hollis-Eden and the nuclear threat.

Recently, the head of the Domestic Nuclear Detection Office at the Department of Homeland Security, Vayl Oxford, stated, "I tell my people, assume there is a 100 percent chance someone will try to attack us with a nuclear weapon in the next five to ten years." Similar conclusions have been reached by a number of recent prominent analyses of the threat of a nuclear or radiological attack, including those by Harvard professor Graham

Allison, the Monterrey Institute, and the Nuclear Threat Initiative, headed by former Senator Sam Nunn.

Contrary to popular belief, the majority of the victims of a nuclear attack would die not from the blast, but from Acute Radiation Syndrome (ARS). They will die over the next two weeks from Acute Radiation Syndrome or ARS. ARS kills by damaging the bone marrow; victims are killed by white blood cell loss and opportunistic infection or bleeding out from platelet loss. The British Medical Journal recently estimated that a 12.5 kiloton bomb detonated in New York City would kill at least 50,000 people instantly. But another 200,000 would be expected to die later from ARS and sicken an additional 700,000 more from the affects of ARS.

Imagine if you could treat ARS with a low cost, self-administered, non-toxic, stable drug that had no side effects. You could literally save hundreds of thousands of lives. You could protect first responders who could then be sent in to conduct rescue and relief efforts. You could substantially decrease the burden on a health care system that will be overwhelmed. And, most importantly, you could dramatically reduce the incentive—the level of terror—that drives terrorists like Osama bin Laden to seek to use nuclear weapons.

In fact, we can. Hollis-Eden is developing a drug called HE2100 or NEUMUNE. This drug works by boosting the body's own innate immune system. To date, results of test in over 200 non-human primates treated with NEUMUNE demonstrated the drug to be safe and effective in the treatment of ARS. In one recent trial, 90 percent of the treated primates survived otherwise lethal doses of radiation, while only 55 percent of the untreated group survived. Extrapolating these results using the numbers of people who will be exposed to ARS in a nuclear attack on a major American city shows the dramatic effect this drug could have in reducing the number of casualties in such an event.

There is no other drug available now or in the development pipeline that can treat ARS.

However, in practice, developing such a counter-measure is no small task. It takes over ten years and hundreds of millions of dollars to develop a new drug. In our case, Hollis-Eden has spent and continues to spend tens of millions of dollars to fund expensive trials and other development costs conducted by AFRRI and elsewhere. In fact, we have spent over $100 million to develop NEUMUNE, and we are on the verge of spending millions more for the required manufacturing scale up process, pivotal efficacy and safety trials for the drug to qualify for approval, which we anticipate filing for in 2006

Only one-in-ten drugs that enter the Food and Drug Administration (FDA) approval process are ever approved. At the same time, the operating margin for successful biopharma companies is 2.76 to 3.74 times the operating margins for major defense contractors. In other words, the opportunity cost for a biotechnology company considering pursuing a medical counter-measure is extremely high. And, most pharmaceutical companies—and as importantly their investors—are reluctant to pursue a

market that has only one likely customer, particularly where that customer is the federal government.

A recent report by the American Venture Capital Association, a consortium of the private investors who fund emerging biotech companies, determined that the pharmaceutical industry hasn't invested in biodefense because the market has only one customer (the federal government), offers lower than average profit margins, is fraught with political vulnerability, and is plagued by uncertain liability and patent protection. Fittingly, this report is entitled, "Government Market Enigma Causes Industry to Stick with What They Know."

Against this backdrop, most pharmaceutical companies have continued to invest their time and resources to finding new cures for cancer, premature baldness, erectile dysfunction and more obviously lucrative efforts.

However, it is important to underscore that industry isn't the problem here—in fact, as I will discuss later, it is the solution. Most pharmaceutical companies are publicly traded. Those of us who run these companies have a fiduciary duty to our investors to maximize shareholder value. As the Michigan Supreme Court said in the seminal case *Dodge v. Ford Motor Company* a "business corporation is organized and carried on primarily for the profit of stockholders" and that "[t] he powers of the directors are to be employed for that end." This understanding is vital to developing a fully effective BioShield program.

At the same time, the federal government has no expertise in drug development. Various federal agencies, such as the National Institutes of Health, fund and conduct outstanding basic research. However, while basic research can produce knowledge that may identify ideas for new drugs, such research is a far cry from the business of actually developing a drug, taking it through pre-clinical and clinical trials, and then through the rigorous Food and Drug Administration approval process. Moreover, given the costs of drug development—hundreds of millions of dollars in sunk costs—the federal government's present day biodefense budget cannot afford to pursue the vast numbers of promising medical counter-measures to the multitude of threats our nation faces today—to say nothing of the dangers of new bioengineered threats we may face tomorrow.

Put simply, this nation needs a biodefense capability and for that effort to be effective it must foster an engaged, focused private sector biodefense industry.

Recognizing this, in 2004, the President and Congress enacted BioShield. BioShield was intended to provide the private sector with a series of market-based incentives to encourage the pharmaceutical industry to focus on developing new medical counter-measures.

The bill as described by Dr. Mark McClellan, then-FDA Commissioner, at the 2003 BIOCEO conference was very straightforward and simple to understand for interested companies and investors. He described the process as one in which the secretaries of HHS and DHS would collaborate and agree on the major chemical, biological,

radiological and nuclear (CBRN) threats and unmet medical needs to those threats. Once the threats were established, the secretary of HHS and his department would then assess what type of medical countermeasures were needed to address that threat. During the scientific assessment of new technology if the scientific experts thought it was feasible to develop such a countermeasure within eight years, the federal government would enter into an advanced purchase contract with that company committing the federal government to buy the product upon successful FDA approval. Dr. McClellan went on to emphasize that BioShield advance purchase contracts must be of a size and scope—"hundreds of millions of dollars"—in order to encourage the industry to participate and to justify their investment in biodefense product development.

The statutory framework described by Dr. McClellan is based on three groundbreaking changes to how the federal government purchases medical counter-measures. And, I would argue more broadly that these changes offer a model for how to encourage more innovative and entrepreneurial behavior in government procurement writ large.

Defining the market: Under the statute the Department of Homeland Security (DHS), in conjunction with the Department of Health and Human Services (HHS), was charged with identifying the series of threats for which the federal government was seeking to purchase medical counter-measures. This process is known as the "Material Threat Assessment" or "MTA." In economic terms DHS was charged with defining the market: we need X million treatments for threat A, Y million for threat B, and so on.

Providing early market incentives and shifting risk: Under the BioShield law, HHS was then authorized to enter into early stage advance purchase contracts with companies that presented something more tangible than a good idea as to how to address one of the priority threats. Under the terms of these contracts, the company would only get paid if they produced a drug that was capable of being stockpiled and ultimately FDA approved. In other words, HHS would not be responsible for funding the development of these drugs, nor would the agency be out anything if the prospective drug failed to work. These protections are critical in an industry where only one-in-ten drugs receive FDA approval.

On the other hand, by offering at an early stage binding terms, such contracts were intended to allow the company to go to the private sector to obtain the capital necessary to develop its promising drug. As Dr. McClellan said the size of these contracts would be such that they would provide companies with ROI sufficient to justify investing in this space to their shareholders and other investors. Investors, aware of the specific market and the potential return on investment if the company was successful in developing the drug, would do their due diligence and based on their analysis decide to invest or not. Companies that were seen as having the ability to deliver would be able to raise more than sufficient private capital to fund drug development without having to wade through a slow and bureaucratic taxpayer funded grant process.

Under this paradigm envisioned by the BioShield Act, government would be able to shift the heavy risk of drug development from the taxpayer to the informed investor and the

pharmaceutical companies. If a drug failed the taxpayer would have lost nothing and the burden of risk and return is on the investor.

It would also allow HHS the ability to leverage the relatively small amount of funding it was provided for BioShield. The Tufts Center for the Study of Drug Development estimates that industry expends more than $800 million on average to develop a new chemical entity. With initially only $5.6 billion in guaranteed markets for BioShield products, BioShield monies need to leverage private investment if the program is to work. (By way of comparison, the federal budget for missile defense—for a system designed to thwart a Cold War era threat, not today's threats—is just under $7 billion per year).

BioShield as proposed and signed by the President and enacted by Congress is a groundbreaking, market-based, highly innovative, entrepreneurial-focused, federal procurement program.

II. Implementation Issues Undercut BioShield's Ability to Succeed and Serve as an Entrepreneurial, Market-Based Procurement Program

However, the program has not been implemented in a manner consistent with that vision.

First, the markets remain undefined: During a recent hearing on BioShield before the Before the House Subcommittee on Emergency Preparedness, Science and Technology of the Committee on Homeland Security, Michael Greenberger, Professor of Law and Director of the University of Maryland Center for Health and Homeland Security testified that:

> The [BioShield] Act established no procedure for DHS to employ in supervising the making of the material threat determinations. Despite what was an obvious Congressional invitation to summarily determine what are the widely recognized [WMD] threats to the United States, DHS has employed an opaque, highly bureaucratized, relatively lengthy process for determining material threats. Over the course of the past year, this cumbersome and poorly delineated administrative process has led to only four material threat determinations. Findings have been made that Anthrax, Smallpox, Botulinum toxin and radiological/nuclear devices pose a material threat to the United States. DHS officials have promised that by the close of this fiscal year material threat determinations will be made concerning plague, tularemia, and viral hemorrhagic fevers . . . . DHS's lassitude in supervising the making of material threat findings is mystifying. The legislative history of the statute is replete with references to a myriad of agents, beyond the four agents identified, posing a substantial threat to the United States.

The American Venture Capital Association, a consortium of the investors who fund early-stage biotech companies, recently issued a report entitled "Government Market Enigma Causes Industry to Stick with What They Know." This investors' report concluded that biodefense is not an open market and the field is "politically charged with shifting priorities." This is not the sort of defined market environment that will attract industry involvement.

Second, HHS hasn't incorporated "the market" into their thinking: Capital markets react to everything and they do so in very real time. These markets are based on expectations—expectations of performance and timing being the two most important factors. Some may argue that on occasion these expectations are unrealistic, however, that isn't the point. Whether reasonable or unreasonable, in order for BioShield to be effective, it needs to harness the markets, not work against them. In order to do so, HHS has to understand how the markets act and react. To date it has not.

The experience of my company provides a concrete example of how this has undercut efforts to develop new drugs to protect the American people from terrorist threats.

Two weeks after the devastating September 11, 2001 attacks on our country, officials from the Armed Forces Radiobiology Research Institute ("AFRRI"), a research division of the Department of Defense, approached Hollis-Eden and informed us that they wanted to fast track the development of one of our experimental drugs for the treatment of ARS.

Given that our product is the single available treatment for the single greatest threat our nation faces, one would assume that HHS has moved with all possible speed to procure this drug. However, four years after 9-11 and AFRRI's entreaty to us, and a year after the passage of BioShield and at this time we do not have a contract. In fact, there isn't even a final RFP out for a nuclear medical counter-measure.

DHS has provided HHS with the required MTA. In October of 2004, HHS put out a request for information to assist the agency in procuring a drug for ARS. Our information leads us to believe that we will be the only fully qualifying bidder. As a result of the information provided under the RFI, HHS is well aware of what interest there is in this procurement and what potential therapies may be offered to it under a RFP. As a result, it would be entirely appropriate for HHS to make use of the authorities under Project BioShield, or even the typical-FAR authorities, to award a contract to Hollis-Eden as quickly as possible. While there are other products that purport to treat ARS, they are in very early stage of development, only beginning the regulatory process for licensure. Moreover, they are being produced by more or less "virtual" companies that have spent less than $300,000 in the development of their purported treatments based upon public filings. Thus, the very idea that HHS will conduct a competition for a product it knows has no comparable equivalent simply does not make sense. However, HHS has not moved to issue the RFP, let alone move to a sole source contract.

On May 20 of this year, the Department of Health and Human Services issued a Special Notice, advising of its intent to issue a Draft Request for Proposals by the end of July 2005 to acquire a drug for the prevention and/or treatment of Acute Radiation Syndrome.

At a recent hearing of the House Government Reform Committee on BioShield implementation, Chairman Davis derisively likened this additional Draft RFP interim step to the high school-esque relationship of "being engaged to be engaged."

Long delays, such as the one we have faced, are now routine in BioShield procurement efforts and they have sent the markets the wrong signal. The investor community sees these delays and reads into them that the federal government is simply not serious about procuring drugs for WMD threats and, generally speaking, developing a BioShield industry.

Again allow me to use Hollis-Eden experiences to illustrate this point. Since 9-11 our company has focused on the development of a drug to address the greatest threat to this nation. At the outset this brought enormous amounts of positive attention on the company. The investor community felt certain that the federal government would leap at the chance to protect the American people from a nuclear attack—it seemed a "no brainer." Recall, immediately after 9-11 the Department of Defense came to us asking us to develop this drug for homeland security. Our stock rose on this positive attention.

Over the course of the next three years we have made extraordinary scientific strides in developing our drug. First, we demonstrated 100 percent survival rates in mice after lethal doses of radiation. Then, we demonstrated up to 90 percent survival rates in primates after lethal doses of radiation—the first drug ever to show an ARS survival benefit. Our IND with FDA was recently approved to initiate human safety studies in the U.S.. In short, we have consistently achieved the major milestones required of the company. If we had shown similar progress in treating any number of other diseases—cancer or heart disease, for example—our stock would be soaring.

However, because the investor community thought procurement of a nuclear medical counter-measure was a "no brainer," HHS' delays and other mixed messages caused uncertainty. This, coupled with the general lack of confidence in biodefense, has caused Hollis-Eden to lose more than $600 in market cap.

And, we are not alone. BioShield was intended to stimulate the biodefense sector. However, since BioShield's passage—with limited exceptions—every company that is active in this sector has seen their share price drop.

Aethlon Medical is developing viral filtration devices that rapidly reduce the presence of infectious disease and toxins in the body that was used in the wake of the anthrax attacks. In March of 2004, in anticipation of BioShield, Aethlon's stock was trading in the $2.75 range. Delays in passing BioShield drove the share price down. At the time of BioShield's passage Aethlon's stock was trading around $1.02. Since BioShield's passage their share price has steadily eroded. Aethlon is now trading in the $.225 range.

MDM Group is developing WMD vaccines and screening products. Like Aethlon, its shares peaked in early 2004 on BioShield anticipation. At the time its stock price broke the $4 mark. By the time of BioShield's passage the stock was in the $2.65 range. It is now trading in the $1.22 range.

Avant Immunotherapeutics is developing biodefense vaccines. In early 2004 its shares traded at just under $4.00. By the time of BioShield's passage its shares were trading around $1.39. Now its stock is trading in the $1.35 range.

Acambis is developing vaccines for infectious diseases such as West Nile and typhoid. The company is currently under contract by the National Institutes of Health to develop a new smallpox vaccine. It shares also peaked in early 2004 around $60. The company then split its stock. As would be expected, their share price dropped, and then rose, but then it began to decline again. By the time BioShield passed, Acambis' shares were trading in the $13.30 range. Today the stock is trading around $8.25.

Clearly there is a disturbing pattern here. And, this is to say nothing of the scores of smaller biotech companies that are trying to break into this market with exciting products but cannot obtain investor money because the market is reticent to back BioShield companies without defined markets, clear timelines, and known not unknown risks.

Put bluntly, the program is having exactly the opposite effect of what was intended. This is particularly sad as BioShield has enormous promise to both safeguard our nation and revolutionize government procurement to a more entrepreneurial, market-based approach.

Third, HHS has failed to utilize the market incentives that are at the heart of the program: To date HHS has only extended a form of advance purchase contract in only one instance: the purchase of a next generation anthrax drug. Instead, according to testimony given by Senator Joseph Lieberman, HHS will not even consider extending a contract for a BioShield drug until the FDA has granted an IND. Senator Lieberman further testified that:

> This interpretation makes no sense and may substantially inhibit the effectiveness of BioShield. The concept behind BioShield is that the government will provide detailed specifications regarding the market for a medical countermeasure so companies can assess whether to risk their capital to develop the countermeasure. This concept applies to research and procurement of any medicine, including those that are long-term research projects that might take many years to reach the IND stage.

Senator Lieberman was one of the two main proponents and primary drafters of the BioShield statute. His view that the IND trigger is not in keeping with the legislative intent should carry great weight.

Moreover, an IND starting line is particularly inappropriate given the nature of the WMD drug development and approval processes. Unlike most drugs, WMD drugs cannot be tested on humans. Instead, WMD drugs are reviewed under the "Animal Efficacy Rule." Under this rule, a WMD drug must show efficacy in nonhuman primates, safety in humans, and similar biochemical responses to the drug in humans and nonhuman primates. As a result, by the time an IND is filed for a WMD drug, the drug is, in most instances, at or near the very end of its development and approval processes—almost all the risks inherent in developing the drug have been taken, and almost all the investments required to fund development have been made. In other words, HHS is intervening so late in the process that its procurement decisions are not encouraging investment in the companies developing BioShield drugs or in the sector as a whole. Rather than driving the market, HHS is riding the market—and this added weight risks breaking the back of the biodefense industry.

BioShield was designed to provide early market signals to encourage the private sector to invest in—and bear the risks of—developing new drugs for WMD threats. However, BioShield increasingly seems to be reverting back to a more traditional government-funded research and development program, one in which HHS selects specific grant recipients to fund experimental development efforts. The risk of a government grant model is two-fold: First, only one-in-ten potential drugs ever receive FDA approval and make it to market. If HHS utilizes Project BioShield to focus on drug development and not procurement, as might appear to be the case thus far, the odds are against picking drugs that will ultimately make it into the Strategic National Stockpile. Second, if HHS picks winners and losers at the early development stage, the industry as a whole will not expend its potentially vast sums of private R&D capital to develop these products for the federal government. Instead, this will become a niche market made up of just a few NIH/HHS companies dependent on federal research grants. As a result, the breadth of technology, knowledge and discovery that will be focused on safeguarding this nation will be only a fraction of what a broader, private sector-based program would provide.

Fourth, HHS has not created an effective, transparent partnership with industry: While I know there are sometimes national security concerns that must be borne in mind when publicly discussing these issues, the fact of the matter is that it has been extraordinarily difficult, if not impossible, to find out anything about this process or about how we, as a small biotech company, might contribute to it. It truly has been very much a "black box" process, and one that we have had to hire several outside consultants to even begin to understand. HHS should now publicly indicate the threats for which it intends to buy products, along with reasonable information about the potential size of the order, the requirements for the products, and approximately when the order will occur. And then HHS should affirmatively open a dialogue with the pharmaceutical and biotechnology industries and with individual companies. This is as obvious as it is true, without better communication with industry, Project BioShield will very simply fail.

III. Putting BioShield Back on Track

Luckily, the program as a whole is conceptually sound. For Project BioShield to be effective and stimulate private companies and investors to participate it simply needs to be implemented the way the law was written.

DHS and HHS have to swiftly define the threats for which the government is seeking to purchase medical counter-measures. To achieve this, the MTA process needs to be dramatically streamlined. By defining these threats, the government will help define the markets for companies and investors. This will allow companies to know what the government wants, when it wants it, and how much of it will be needed.

In reality, however, an MTA isn't a market, it is the promise of a market. In BioShield and other federal procurement efforts there is no market until the lone customer steps up to the plate. Hollis-Eden knows this better than most. As a result, HHS has to then significantly speed the release of RFP's for these drugs. Having witnessed BioShield's problems to date, the markets are not ready to respond on just a MTA for a threat; the markets are waiting to see RFP's—the promise of true contracts.

HHS also must be more open with companies that approach it with innovative treatments for these threats where RFP's may not be issued or where the particular drug does not easily fit an issued RFP. If HHS is only willing to look at one specific way to address one specific threat, one at a time, we may never get past the first threat or two. It can take years to find a treatment for a specific disease. We still don't have a cure for the common cold—and not for a lack of trying. In a perfect world there would be scores of open RFP's—corresponding to the multitude of serious threats we face—on the street waiting for companies that think they have a solution.

HHS should also be much quicker to issue RFP's to promising technologies—at times even issuing multiple RFP's on a single threat and creating a competition among companies. Remember, using the BioShield procurement process doesn't cost the taxpayer anything until a company delivers a safe and effective treatment for a weapon of mass destruction.

In addition, if HHS wants to engage the pharmaceutical industry as a whole in BioShield-related research and drug development, the contracts issued under the program need to be of sufficient size and provide adequate returns on investment to allow these companies to justify BioShield investments to their investors. As then-FDA Commissioner Dr. McClellan emphasized in 2003, BioShield advance purchase contracts must be of a size and scope—"hundreds of millions of dollars"—in order to encourage the industry to participate and to justify their investment in biodefense product development.

IV. Conclusion

The United States has the most innovative, persistent and effective pharmaceutical industry by far of any country in the world, and we have only begun to unleash that

amazing potential for the protection of the American people from acts of terrorism. It is difficult to navigate and steer at the same time. And, in the case of BioShield, the government, industry and the investor community are literally drawing the map, while trying to determine a course, at the same time we all have a hand on the ship's wheel trying to steer. As a result the program has yet to achieve its full promise. However, with a few mid-term course corrections the full potential of BioShield can be realized.